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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/527,919 | 03/17/2000 | Steven Neville Chatfield | KCO1002US | 3175 |

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| EXAMINER |
|---|
| LI, BAO Q |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1648 | 22 |

DATE MAILED: 12/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

| Advisory Action | Application No. 09/527,919 | Applicant(s) CHATFIELD, STEVEN NEVILLE | |
|---|---|---|---|
| | Examiner Bao Qun Li | Art Unit 1648 | |

*--Th MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

THE REPLY FILED 13 November 2002 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 4 months from the mailing date of the final rejection.

~~b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).~~

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12/16/02

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☒ Applicant's reply has overcome the following rejection(s): *112 1st paragraph*.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *it cannot overcome the obvious type rejection (see attachment)*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: *None*.

   Claim(s) objected to: *None*.

   Claim(s) rejected: *35-38,40-44 and 46*.

   Claim(s) withdrawn from consideration: *None*.

8. ☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)( PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

Bao Qun Li

**Advisory Action**

Claims 35-38, 40-44 and 46 are pending.

The response to the final action filed on October 31 under 37 CFR 1.116 has been entered. Claims 39 and 45 have been canceled. Claims 35, 38, 41 and 44 have been amended. However, the amendment of the claims has been considered but is not deemed to place the application in condition for allowance.

For purpose of appeal, the status of the claims is as follows:

**Allowed claim(s): NONE.**

**Rejected claim (s): 35-38, 40-44 and 46.**

**Claim(s) objected to: NONE.**

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 35-38, 40-44 and 46 are still rejected under 35 U.S.C. 103(a) on the same ground as stated in the previous Office Action as being unpatentable over Mimms et al. (EP-A-0 389 983), Khan et al. (WO 94/03615) and Shi et al. (Vaccine 1995, Vol. 13, pp. 933-937).

Applicants argue that there is no obvious reason why a skilled person would have focused simultaneously and specifically on the disclosure about fragment C in Khan et al. and the disclosure about pre-S1 in Mimms et al. and on the disclosure in Shi et al. Secondly, it was not reasonable predictable that the claimed fusion proteins would produce a good antibody titer against the pre-S1 sequence.

Applicant's arguments have been fully considered but they are not persuasive because the tet fragment C used as a carrier protein with different antigens has been known in the art as evidenced by Khan et al., they explicitly teach that has been extensively used as an adjuvant and

recombinant antigen made by Tetanus toxoid C (tetC) has been shown to have good and enhanced immunogenicity (line4 on page 3 through line 8 on page 4). Khan et al. also point out that several viral antigens, such as HIV, hepatitis A or B et al. are suitable for making a fusion protein with tetC as a good vaccine candidate for inducing a protective immunity against HBV (page 5, line 10 through page 6, line 4).

Mimms et al. teach several epitopes of HBV pre-S1 protein as a subunit antigen to be able to induce immune response against HBV pre-S1 or Pre-S2 for as antigens to produce the anti-pre-S1 and pre-S2 antibodies (see example 4).

Therefore, it would have been obvious by combining the teaching of Khan et al. and Mimms to produce an enhanced immune response without unexpected result. .

The additional reference of Shi et al. further support the possibility of making HBV subunit antigen as a fusion protein with a cholera toxin B, CTB to stimulate the immune response.

Applicants are reminded that the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

Since there is no unexpected results, it is still concluded that the claimed invention as a whole is prima facie obvious absence unexpected results.

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 703-305-1695. The examiner can normally be reached on 8:00 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Bao Qun Li

December 2, 2002

James C. Housel

JAMES HOUSEL 12/16/02
SUPERVISORY PATENT EXAMINER
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